Sustainable synthesis of uridine-5’-monophosphate analogues by immobilized uracil phosphoribosyltransferase from Thermus thermophilus

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Abstract

Nowadays enzymatic synthesis of nucleic acid derivatives is gaining momentum over traditional chemical synthetic processes. Biotransformations catalyzed by whole cells or enzymes offer an ecofriendly and efficient alternative to the traditional multistep chemical methods, avoiding the use of chemical reagents and organic solvents that are expensive and environmentally harmful. Herein we report for the first time the covalent immobilization a uracil phosphoribosyltransferase (UPRT). In this sense, UPRT from Thermus thermophilus HB8 was immobilized onto glutaraldehyde-activated MagReSyn®Amine magnetic iron oxide porous microparticles (MTtUPRT). According to the catalyst load experiments, MTtUPRT3 was selected as optimal biocatalyst for further studies. MTtUPRT3 was active and stable in a broad range of temperature (70–100 °C) and in the pH interval 6–8, displaying maximum activity at 100 °C and pH 7 (activity 968 IU/gsupport, retained activity 100%). In addition, MTtUPRT3 could be reused up to 8 times in the synthesis of uridine-5’-monophosphate (UMP). Finally, MTtUPRT3 was successfully applied in the sustainable synthesis of different 5-modified uridine-5’-monophosphates at short times. Taking into account these results, MTtUPRT3 would emerge as a valuable biocatalyst for the synthesis of nucleoside monophosphates through an efficient and environmentally friendly methodology.

Keywords:

Biocatalysis, Enzyme immobilization, Phosphoribosyltransferase, Nucleic acid derivatives, Active pharmaceutical ingredients